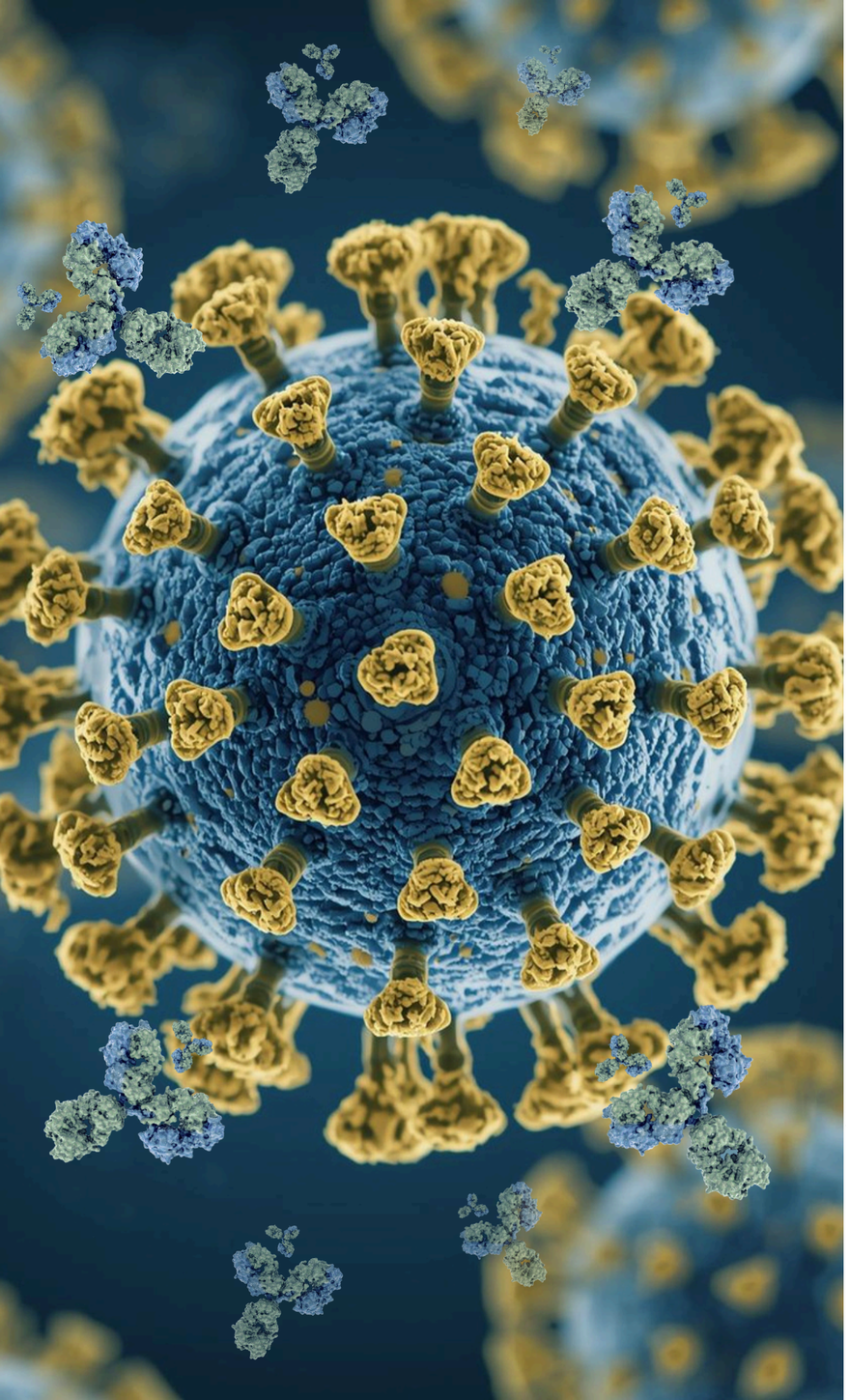

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Protective Immunity to VZV: The Role of Binding and Neutralizing Antibodies

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The 34th Annual Virology Association of Thailand Conference
Viruses across Life's Journey: Old, New, and Unforeseen
17-18 Nov 2025

Outline

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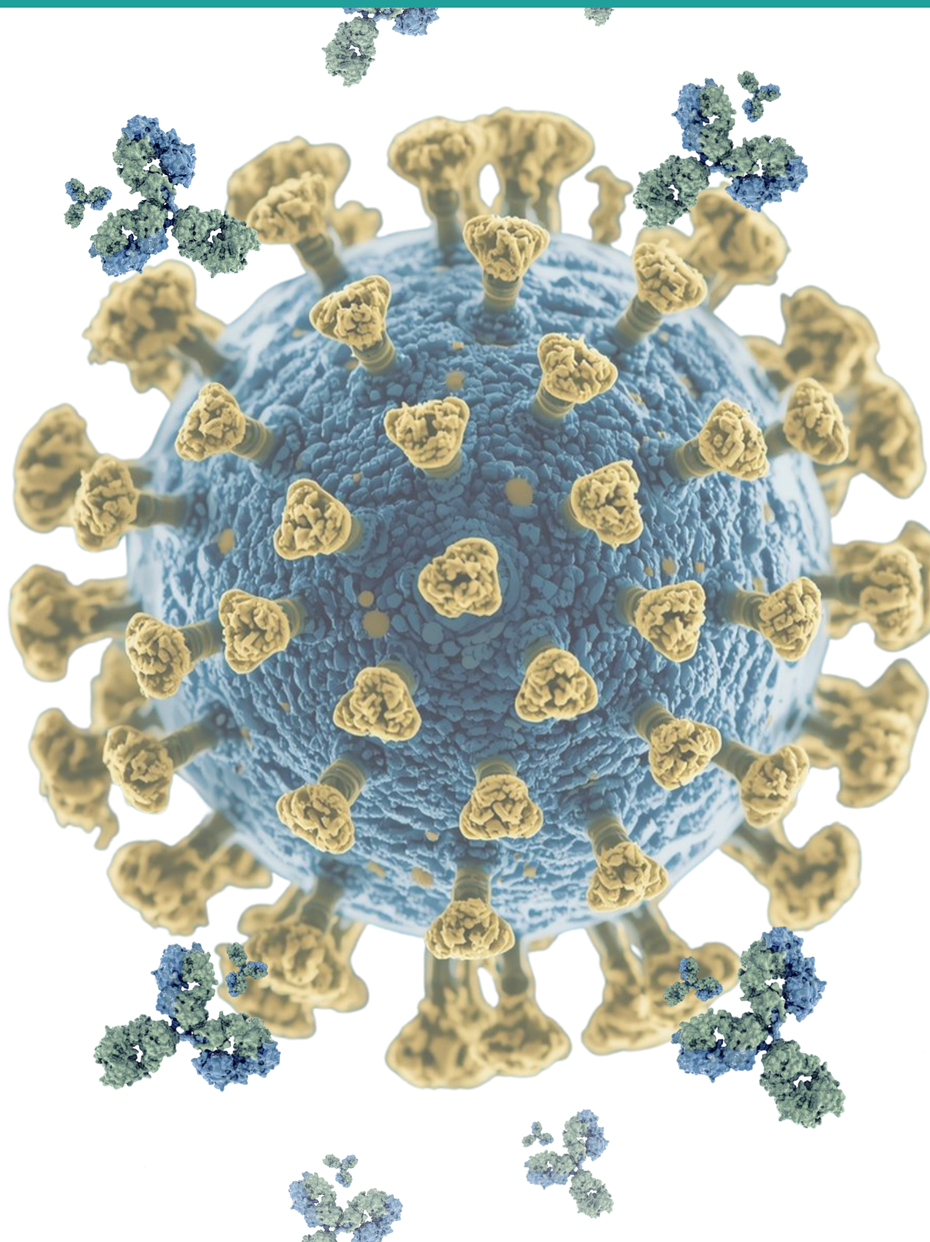
- VZV and Associated Diseases
- VZV Antibodies: Current Knowledge and Knowledge Gaps
- Our Research to Bridge the Gaps
- Future Plan



Varicella-Zoster Virus (VZV)

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- **Family**: *Herpesviridae*
- **Key Features**:
  - Establish lifelong neuronal latency
- **Associated Diseases**:
  - Primary infection: Varicella (chickenpox)
  - Reactivation: Zoster

Chickenpox

https://www.britannica.com/science/chickenpox

Zoster

https://jetem.org/herpes_zoster/

Role of Antibodies (Ab) in VZV

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Clinical evidence: VZV Ab correlates with protection

Administration of varicella zoster immunoglobulin can:

- Prevent chickenpox in exposed children
- Reduce post-herpetic neuralgia in adults by 50%

Lower VZV antibody levels are associated with:

- Higher chickenpox incidence/severity in children
- Higher zoster risk in adults

Habib et. al (2021). Vaccine, 39(25), 3445-3454. Gilbert et. al (2014). The Journal of infectious diseases, 210(10), 1573-1581. Hügler et. al (2002). European journal of pain, 6(6), 435-445.

Ab Response to VZV

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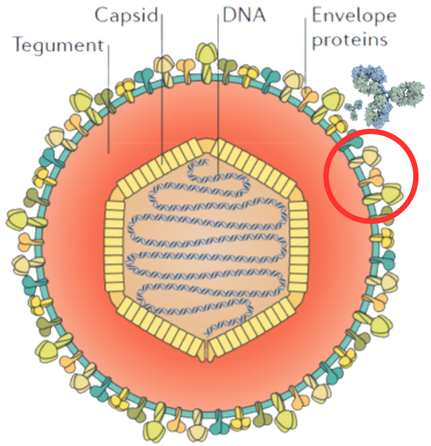

Zerboni et. al (2014). Nature reviews microbiology, 12(3), 197-210.

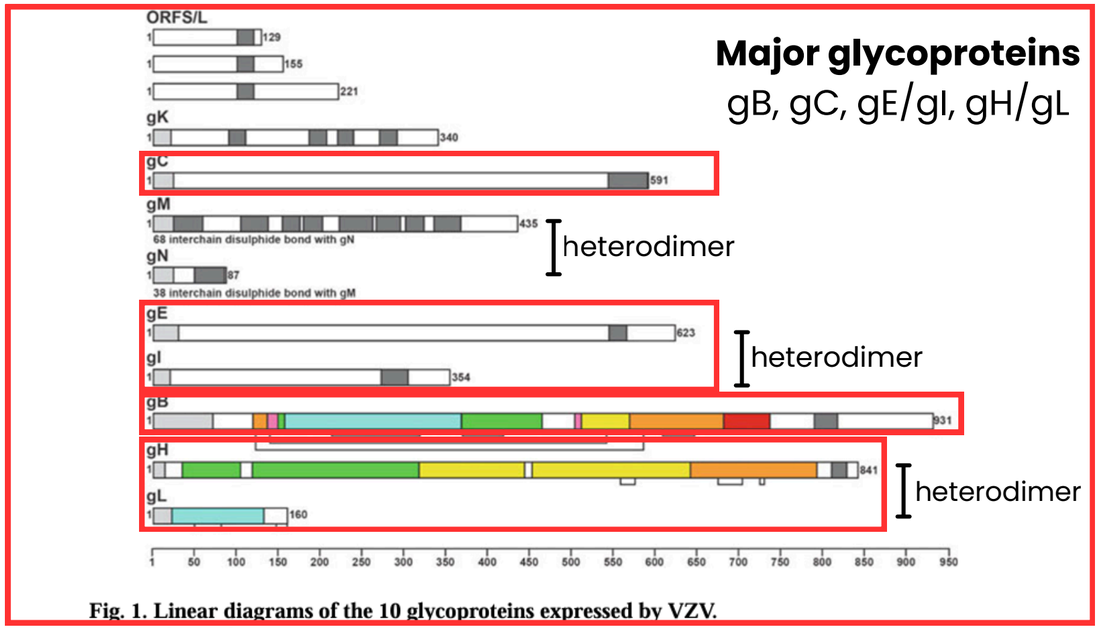

Fig. 1. Linear diagrams of the 10 glycoproteins expressed by VZV.

Oliver et. al (2021). In Varicella-zoster Virus: Genetics, Pathogenesis and Immunity (pp. 25-58). Cham: Springer International Publishing.

VZV glycoproteins (gp): Primary Ab target

Binding antibodies (BAb):

- All Ab against VZV; indicating existing immunity, not protection

Neutralizing antibodies (NAb):

- Subset of BAb blocking VZV entry and infection; confer protective immunity

Binding to neutralizing antibodies ratio (B/N) reflects antibody quality

VZV Serology and Incidence

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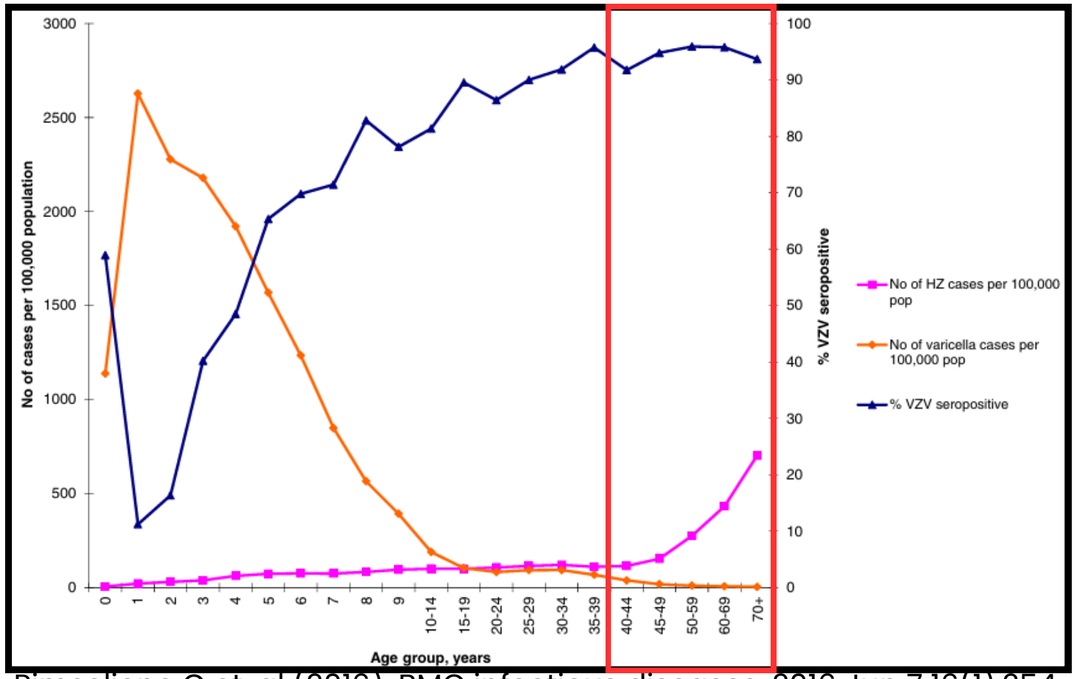
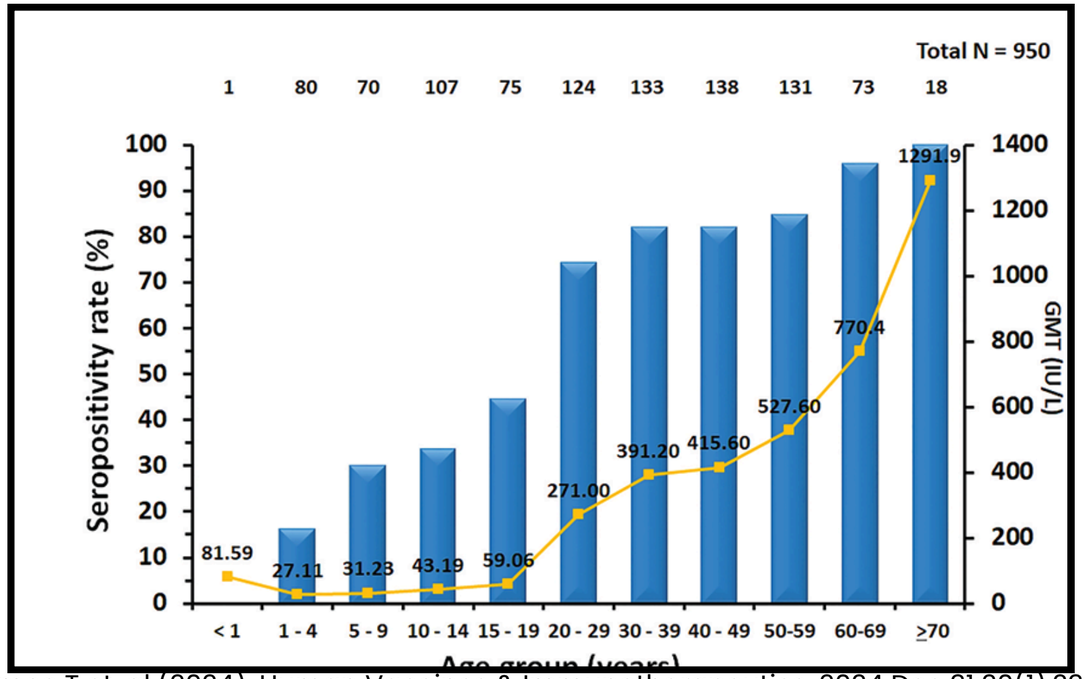


Rimseliene G et. al (2016). BMC infectious diseases. 2016 Jun 7;16(1):254.



Thongmee T et. al (2024). Human Vaccines & Immunotherapeutics. 2024 Dec 31;20(1):2367283.

VZV seroprevalence and antibody level

- Rise with age
- Correlate with chickenpox incidence in children, but not with zoster among the elderly

Bridging the Gaps: Our Research

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Knowledge gaps

Most VZV studies focus on BAb, not NAb or Ab quality, leaving the role of Ab in zoster protection unclear

The impact of aging on NAb or Ab quality (B/N) is unknown

Research questions

Does NAb or Ab quality better predict protection against zoster than BAb?

How does aging affect NAb or Ab quality to VZV?

Hypothesis

Aging impairs NAb or Ab quality, increasing zoster risk despite high BAb levels

Objective

Assess VZV seroprevalence, BAb, NAb, and B/N among Thai elderly

Research Methodology

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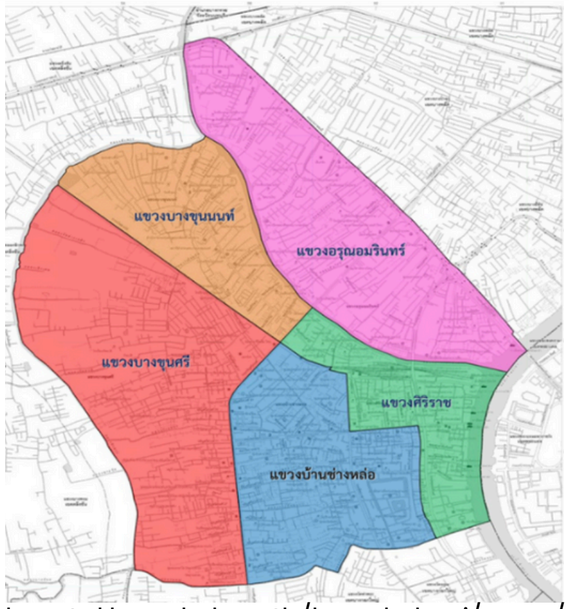

https://webportal.bangkok.go.th/bangkoknoi/page/sub/21955

Study design:

- Community-based cross-sectional cohort

Study population:

- 213 individuals, aged ≥60 years
- From 26 communities in Bangkok-Noi, near Siriraj Hospital

Sample and data collection:

- Blood samples
- Demographic data and zoster history/vaccination

Data and sample collection

Registration → Screening → Physical Examination → Data & Blood Collection

Siriraj Dept. Collaboration: Preventive and Social Medicine, Immunology, and Clinical Pathology

Community outreach for participant screening and enrollment

Research Methodology

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Laboratory Assessment

BAb Measurement:

- gp IgG ELISA (total VZV glycoproteins)
- gH/gL IgG ELISA (highly neutralizing epitope)

NAb Measurement:

- Live-virus microneutralization assay

Data Analysis

Seroprevalence Estimation

Correlation Analysis

- Assess relationships between age and levels of BAb, NAb, and the ratio of B/N

Our Findings: Study Population

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Characteristic	All participants (*N* = 213)
Age (years)	
Median (min–max)	69.0 (60.0–90.0)
Age group, *N* (%)	
60–69 years	111 (52.1)
70–79 years	79 (37.1)
≥ 80 years	23 (10.8)
Gender, *N* (%)	
Male	97 (45.5)
Female	116 (54.5)
HZ history, *N* (%)	
No	182 (85.4)
Yes	30 (14.1)
Unknown	1 (0.5)
HZ vaccination, *N* (%)	
No	206 (96.7)
Yes	3 (1.4)
Unknown	4 (1.9)

Study Participants (n = 213)

Age: 60–90 years

Gender: no gender bias

History of zoster: 85.4% never had zoster

Zoster vaccination: 96.7% never vaccinated

- Vaccine not in national EPI; voluntary & costly → low coverage in high-risk group

Mangmee S et. al (2025).Scientific Reports. 2025 Apr 21;15(1):13776.

Our Findings: Elderly VZV Immunity

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Serostatus	All participants (*N* = 235)	Adult (*N* = 22)	Elderly (*N* = 213)	*p*-value
VZV gp IgG ELISA, *N* (%)				**< 0.001**
Seropositive	229 (97.4)	19 (86.4)	210 (98.6)	
Borderline	2 (0.9)	0 (0.0)	2 (0.9)	
Seronegative	4 (1.7)	3 (13.6)	1 (0.5)	
VZV live virus MNT, *N* (%)				**< 0.001**
Detectable NAb titer	148 (63.0)	6 (27.3)	142 (66.7)	
Undetectable NAb titer	87 (37.0)	16 (72.7)	71 (33.3)	

Undetectable NAb: <1:20 dilution shows no inhibition

Seroprevalence:

- High as 98.6%
- Higher than adults

NAb

- Only 66.7% of VZV-seropositive elderly have NAb

Mangmee S et. al (2025).Scientific Reports. 2025 Apr 21;15(1):13776.

Our Findings: Age-specific VZV-Ab

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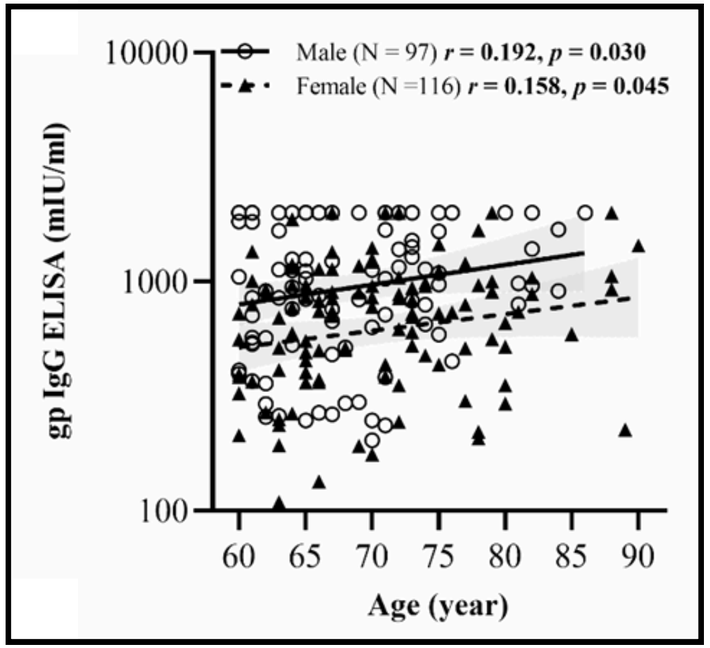
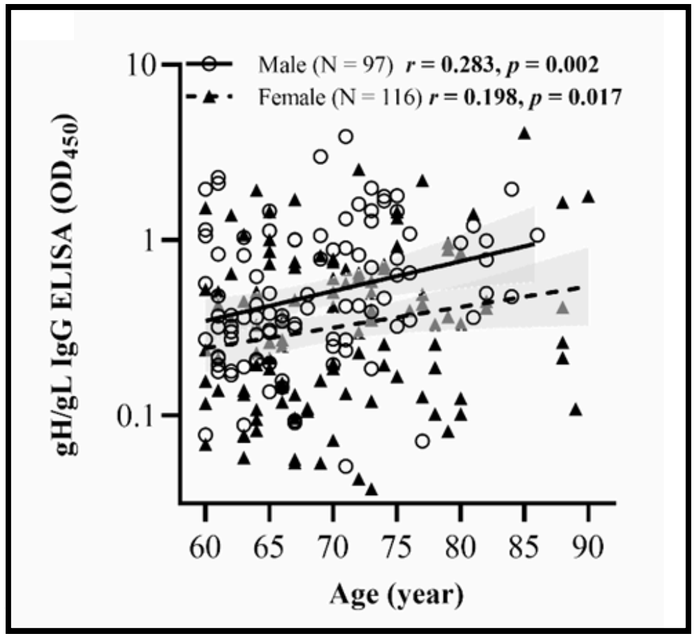
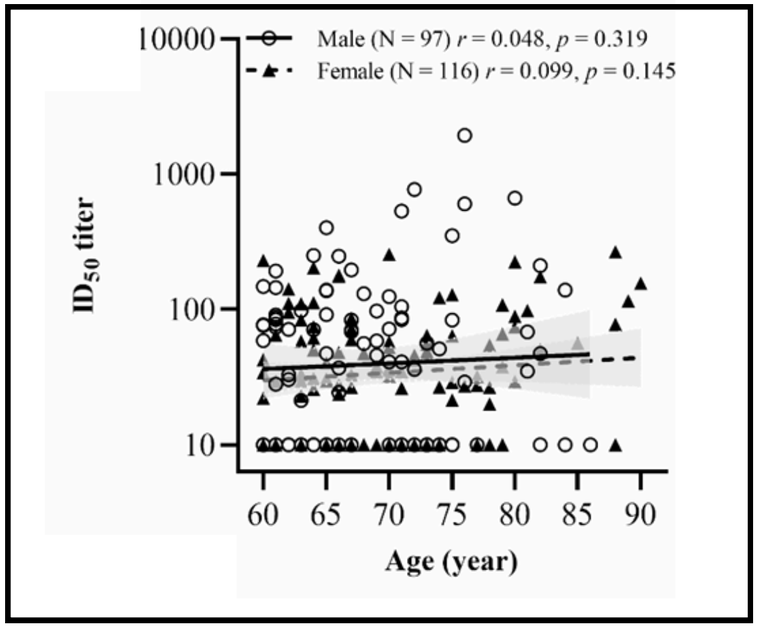
Binding antibodies (BAb)





BAb (VZV gp IgG ELISA, gH/gL IgG ELISA) levels increases with age

Neutralizing antibodies (NAb)



NAb level stable with age

Mangmee S et. al (2025).Scientific Reports. 2025 Apr 21;15(1):13776.

Our Findings:Age-specific VZV-B/N

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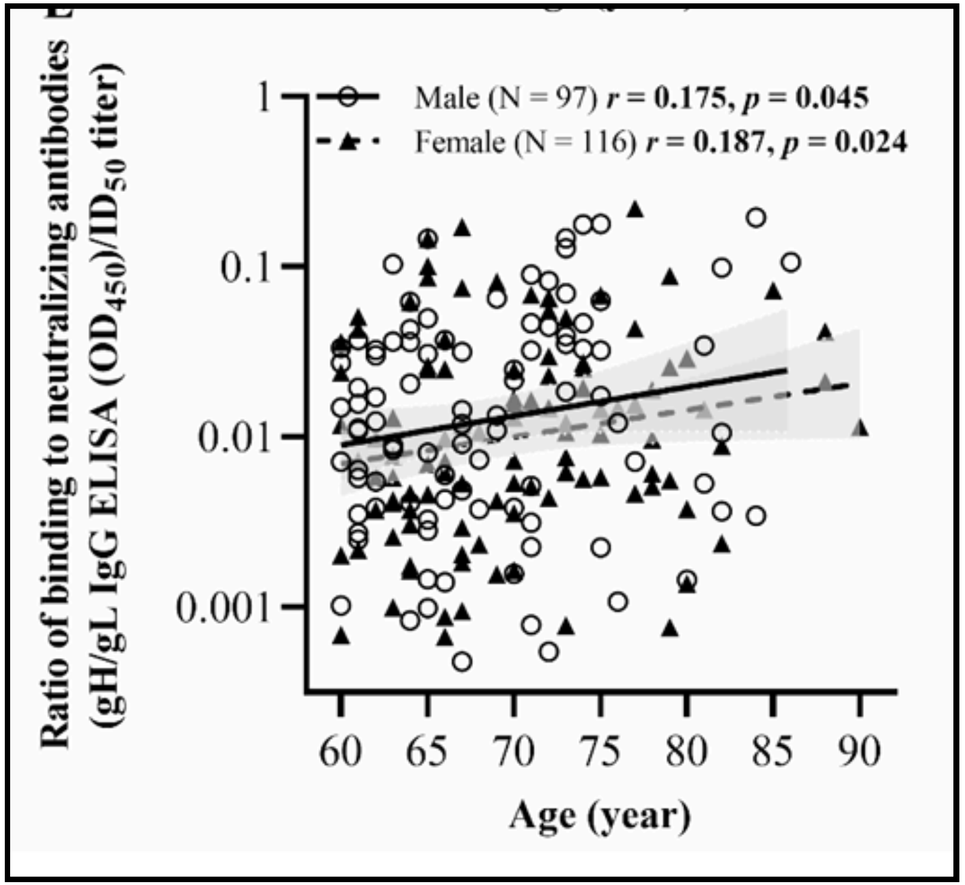

- Increasing B/N ratio with age
- Increasing proportion of non-NAb to VZV-Ab with age in the elderly
- Reflecting reduced Ab quality

At what age does Ab quality decline the most?

Mangmee S et. al (2025).Scientific Reports. 2025 Apr 21;15(1):13776.

Our Findings:Age-specific VZV-B/N

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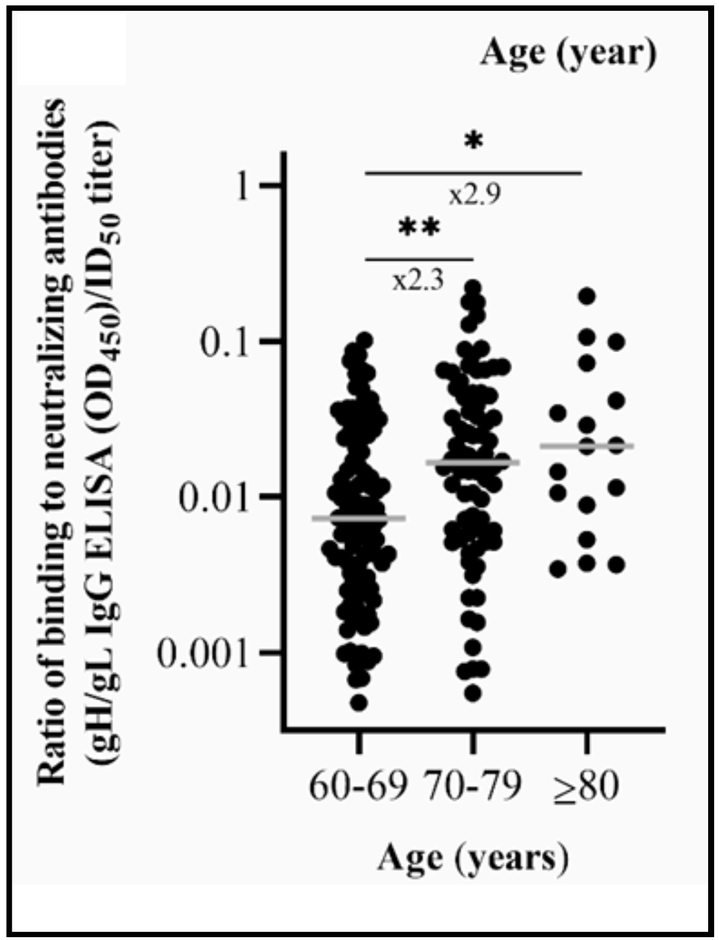

Increase in B/N among the elderly

- 2.3 fold-increase in 70-79 years
- 2.9 fold-increase in ≥80 years
- Elderly age ≥70 years may be the highest-risk group for zoster

Mangmee S et. al (2025).Scientific Reports. 2025 Apr 21;15(1):13776.

Our Findings vs Other Studies

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Consistent with previous studies

- VZV seroprevalence and Ab level (BAb) increase with age

Additional insight from this study

- Ab quality declines with age; a higher proportion of non-NAb in the elderly
- Marked decline in Ab quality in elderly ≥70 years
- This age-related decline may explain the increased incidence of zoster in older adults

Future Plan

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Bridging the population gap:

- **Thai HIV-infected individuals** (highly vulnerable to VZV)
  - Longitudinal characterizing antibody dynamics (quantity & quality) from childhood to adulthood

Acknowledgement

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Siriraj Hospital

Siriraj Research Development Fund

All community leaders and participants

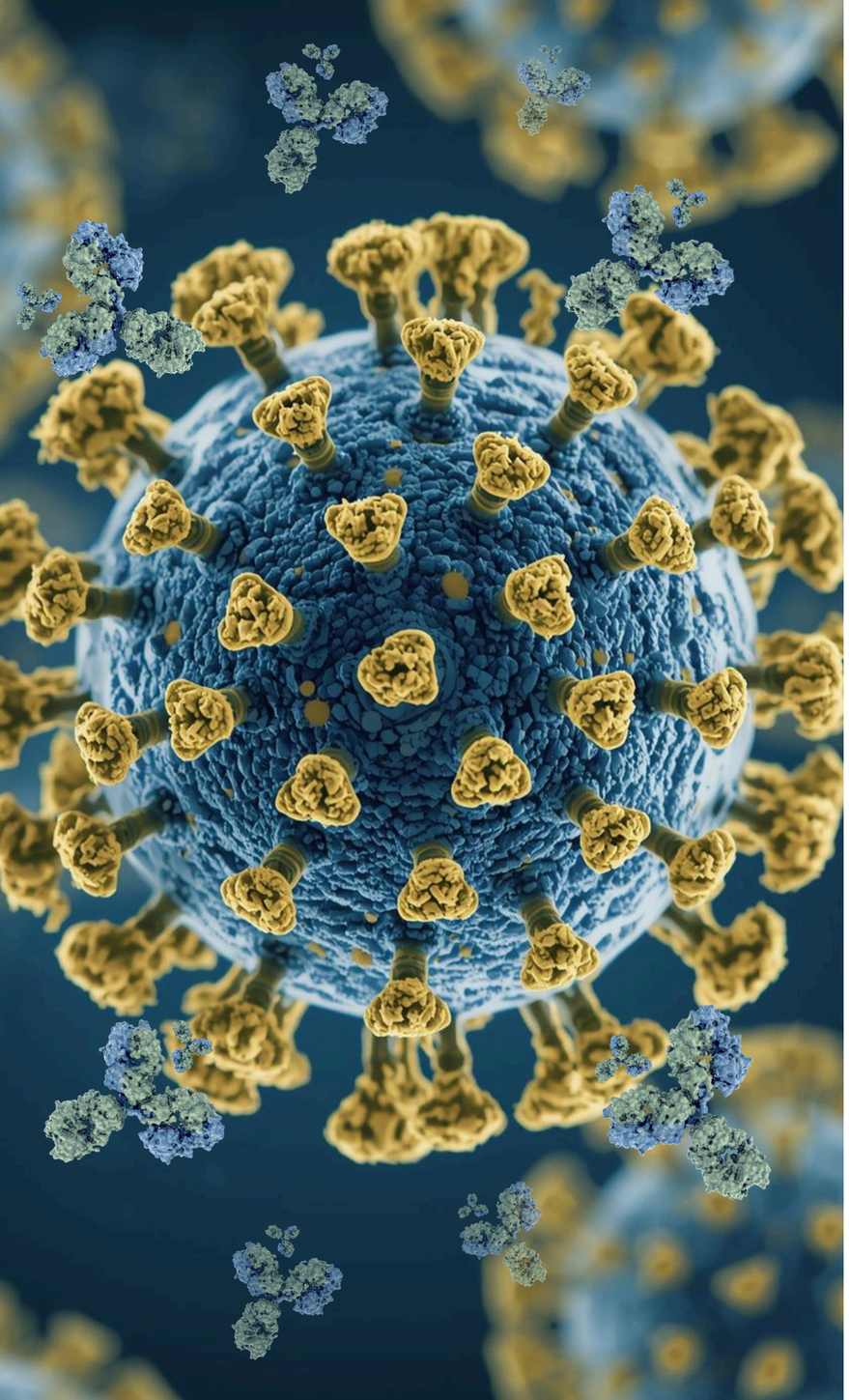
Department of Preventive and Social Medicine
Prof.Prasert Assantachai and all staffs

Department of Immunology
Prof.Dr.Tararaj Dharakul,
Assist.Prof.Dr.Jarupa Soongsathitanon,
and all staffs

Department of Clinical Pathology
All staffs

VIRL
Viral Immunology Research Laboratory

Assoc.Prof.Dr.Kobporn Boonnak and staffs



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THANK YOU

Q&A

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